upadacitinib (Rinvoq™)

Policy # 00692
Original Effective Date: 12/11/2019
Current Effective Date: 01/11/2021

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider the use of upadacitinib (Rinvoq™)‡ for the treatment of adult patients with moderately to severely active rheumatoid arthritis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for upadacitinib (Rinvoq) will be considered when all of the following criteria are met:

- Patient has a diagnosis of moderately to severely active rheumatoid arthritis; AND
- Patient is 18 years of age or older; AND
- Patient had an inadequate response or intolerance to methotrexate; AND
- Requested drug is NOT being used in combination with biologic disease modifying anti-rheumatic drugs (DMARDs), such as adalimumab (Humira®)‡ or etanercept (Enbrel®)‡, OR potent immunosuppressants such as azathioprine and cyclosporine, OR drugs such as apremilast (Otezla®)‡ or tofacitinib (Xeljanz/XR®)‡; AND
- Requested drug may be used alone or in combination with methotrexate or other NON-biologic DMARDs; AND
- Patient has a negative TB (tuberculosis) test (e.g., purified protein derivative [PPD], blood test) prior to treatment.

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When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of upadacitinib (Rinvoq) when the patient selection criteria are not met to be **investigational.***

Background/Overview

Rinvoq is indicated for the treatment of adults with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate. Rinvoq is a Janus kinase (JAK) inhibitor. JAKs are intracellular enzymes which transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function. Within the signaling pathway, JAKs phosphorylate and activate Signal Transducers and Activators of Transcription (STATs) which modulate intracellular activity including gene expression. Rinvoq modulates the signaling pathway at the point of JAKs, preventing the phosphorylation and activation of STATs. The recommended dose of Rinvoq is 15 mg once daily and may be used as monotherapy or in combination with methotrexate or other conventional (non-biologic) disease modifying anti-rheumatic drugs.

Rheumatoid Athritis

Rheumatoid Arthritis is a chronic (long-term) disease that causes inflammation of the joints and surrounding tissues. It can also affect other organs. It is considered an autoimmune disease. In an autoimmune disease, the immune system confuses healthy tissue for foreign substances. Typically first line treatments such as non-biologic DMARDs are used to treat this condition.

Disease-Modifying Anti-Rheumatic Drugs (DMARDs)

Disease-modifying anti-rheumatic drugs are used for the treatment of rheumatoid arthritis as well as other inflammatory conditions. These drugs slow the disease process by modifying the immune system.

- methotrexate
- cyclosporine
- sulfasalazine
- mercaptopurine

- gold compounds

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Rinvoq is indicated for the treatment of adults with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy and safety of Rinvoq 15 mg once daily were assessed in five Phase 3 randomized, double-blind, multicenter studies in patients with moderately to severely active rheumatoid arthritis and fulfilling the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR 2010) classification criteria. Patients over 18 years of age were eligible to participate. Although other doses have been studied, the recommended dose of Rinvoq is 15 mg once daily.

Study RA-I (NCT02706873) was a 24-week monotherapy trial in 947 patients with moderately to severely active rheumatoid arthritis who were naïve to methotrexate. Patients received Rinvoq 15 mg or upadacitinib 30 mg once daily or methotrexate as monotherapy. At week 26, nonresponding patients on upadacitinib could be rescued with the addition of methotrexate, while patients on methotrexate could be rescued with the addition of blinded Rinvoq 15 mg or upadacitinib 30 mg once daily. The primary endpoint was the proportion of patients who achieved an ACR50 (50% or greater improvement) response at week 12. For the primary endpoint at week 12, 28% of patients achieved an ACR50 in the methotrexate group vs. 52% of patients in the Rinvoq group.

Study RA-II (NCT02706951) was a 14-week monotherapy trial in 648 patients with moderately to severely active rheumatoid arthritis who had an inadequate response to methotrexate. Patients received Rinvoq 15 mg or upadacitinib 30 mg once daily monotherapy or continued their stable dose

of methotrexate monotherapy. At week 14, patients who were randomized to methotrexate were advanced to Rinvoq 15 mg or upadacitinib 30 mg once daily monotherapy in a blinded manner based on pre-determined assignment at baseline. The primary endpoint was the proportion of patients who achieved an ACR20 (20% or greater improvement) response at week 14. For the primary endpoint at week 14, 41% of patients achieved an ACR20 in the methotrexate group vs. 68% of patients in the Rinvoq group.

Study RA-III (NCT02675426) was a 12-week trial in 661 patients with moderately to severely active rheumatoid arthritis who had an inadequate response to conventional disease modifying anti-rheumatic drugs (cDMARDs). Patients received Rinvoq 15 mg or upadacitinib 30 mg once daily or placebo added to background cDMARD therapy. At week 12, patients who were randomized to placebo were advanced to Rinvoq 15 mg or upadacitinib 30 mg once daily in a blinded manner based on predetermined assignment at baseline. The primary endpoint was the proportion of patients who achieved an ACR20 response at week 12. For the primary endpoint at week 12, 36% of patients achieved an ACR20 in the placebo group vs. 64% of patients in the Rinvoq group.

Study RA-IV (NCT02629159) was a 48-week trial in 1,629 patients with moderately to severely active rheumatoid arthritis who had an inadequate response to methotrexate. Patients received Rinvoq 15 mg once daily, active comparator, or placebo added to background methotrexate. From week 14, non-responding patients on Rinvoq 15 mg could be rescued to active comparator in a blinded manner, and nonresponding patients on active comparator or placebo could be rescued to Rinvoq 15 mg in a blinded manner. At week 26, all patients randomized to placebo were switched to Rinvoq 15 mg once daily in a blinded manner. The primary endpoint was the proportion of patients who achieved an ACR20 response at week 12 versus placebo. For the primary endpoint at week 12, 36% of patients achieved an ACR20 in the placebo group vs. 71% of patients in the Rinvoq group.

Study RA-V (NCT02706847) was a 12-week trial in 499 patients with moderately to severely active rheumatoid arthritis who had an inadequate response or intolerance to biologic DMARDs. Patients received Rinvoq 15 mg or upadacitinib 30 mg once daily or placebo added to background cDMARD therapy. At week 12, patients who were randomized to placebo were advanced to Rinvoq 15 mg or upadacitinib 30 mg once daily in a blinded manner based on pre-determined assignment at baseline. The primary endpoint was the proportion of patients who achieved an ACR20 response at week 12. For the primary endpoint at week 12, 28% of patients achieved an ACR20 in the placebo group vs. 65% of patients in the Rinvoq group.

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Treatment with Rinvoq 15 mg, alone or in combination with cDMARDs, resulted in a greater improvement in physical function at week 12/14 compared to all comparators as measured by HAQ-DI (Health Assessment Questionnaire Disability Index).

In all studies except for Study RA-V, patients receiving Rinvoq 15 mg had greater improvement from baseline in physical component summary (PCS) score, mental component summary (MCS) scores, and in all 8 domains of the Short Form Health Survey (SF-36) compared to placebo in combination with cDMARDs or methotrexate monotherapy at week 12/14.

Fatigue was assessed by the Functional Assessment of Chronic Illness Therapy-Fatigue score (FACITF) in Studies RA-I, RA-III, and RA-IV. Improvement in fatigue at week 12 was observed in patients treated with Rinvoq 15 mg compared to patients on placebo in combination with cDMARDs or methotrexate monotherapy.

References

1. Rinvoq [package insert]. Abbvie. North Chicago, Illinois. Updated August 2019.

Policy History

Original Effective Date: 12/11/2019
Current Effective Date: 01/11/2021
12/05/2019 Medical Policy Committee review
12/11/2019 Medical Policy Implementation Committee approval. New policy.
12/03/2020 Medical Policy Committee review
12/09/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 12/2021

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and

whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.